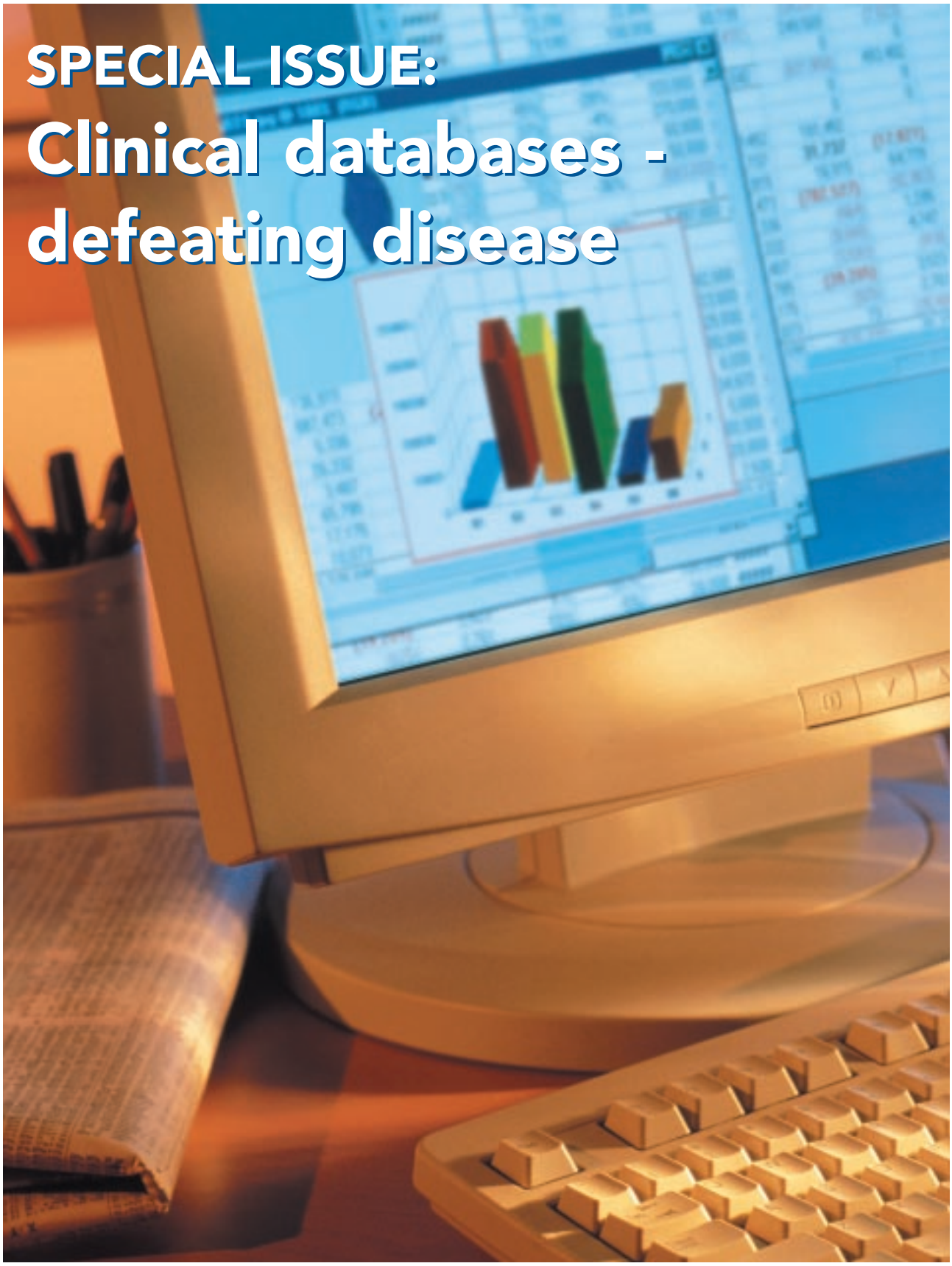
ISSN 0965-1128

THE NEWSLETTER OF THE SOCIETY FOR ENDOCRINOLOGY NUMBER 68 • SUMMER 2003

THE Endocrinologist



SPECIAL ISSUE:
Clinical databases - defeating disease

The Endocrinologist

Society for Endocrinology
22 Apex Court, Woodlands,
Bradley Stoke, Bristol BS32 4JT, UK
Fax: 01454-642222
Email: info@endocrinology.org
Web: www.endocrinology.org

Company Limited by Guarantee
Registered in England No. 349408
Registered Office as above
Registered Charity No. 266813

Deadline for news items for the Summer 2003 issue: **15 August 2003**.
Please send contributions to the above address.

EDITORIAL

'Endocrinologists' greatest vulnerability lies in their capacity to sacrifice an interest in their patients' lives for an obsession with biochemical numbers.' So comments Steve Shalet in this issue's book review (page 12). In so doing, Steve inadvertently provides an important health warning for this special issue on clinical databases!

The introduction of the PC into everyday life has provided the clinician with the ability to collect and analyse vast quantities of data. How best to handle this material is a major challenge. In this issue, the organisers of four sizeable databases of patient information describe their experience of data collection and analysis.

In the excellent and complimentary articles on the HypoCCS and KIMS initiatives (pages 8 and 10), the authors outline the highly successful international collection of safety data on growth hormone-deficient adults treated by hormone replacement. The combined number of patients studied is over 13 000! The authors discuss the importance of large patient numbers in detecting an effect of treatment. Perhaps we, as the general public, should ask how the two databases could work together?

CaHASE and the UK National Acromegaly Database are both national efforts to pool data on uncommon diseases. These are comparatively low budget projects, run through the Society for Endocrinology by its members. You can read more about them on pages 7 and 9. The success of these projects provides a new model for data collection. We hope they will help inform future data-gathering initiatives.

Neural and behavioural development is always a fascinating topic. On page 11, Melissa Hines takes the subject one step further to look at prenatal testosterone's role in determining our lifelong characteristics. This article makes for remarkably clear reading given such a complex issue. Reassuringly, Melissa suggests that 'Human beings appear to be surprisingly flexible with regard to core gender identity'.

We were blessed with wonderful weather at the BES meeting in Glasgow, and I think all will agree that the programme was one of high class science. Doubtless many of you will have spotted the back cover, where the photomontage by Saffron Whitehead, our deputy editor and photographer in residence, will hopefully bring back happy memories for all.

Finally, a reminder that the Society's offices have recently moved (details in the lefthand column of this page). Make sure you send your contributions for the next issue to the new address! Meanwhile, have a good read - don't forget Webspinning (page 6) and look out for details of numerous grants, prizes and awards!

RICHARD ROSS

Basic Science Review Lecture: call for abstracts!

Basic scientists who are no more than 6 years post-PhD should apply now to present a 30-minute review lecture during this year's annual Society meeting. The lecture can be on any endocrine subject (probably a recent or current area of personal research). The Society is offering a £500 honorarium for this prestigious award.

Applicants must be members of the Society for Endocrinology. They should be under the age of 35, although older applicants may be considered in extenuating circumstances (please state if relevant).

Abstracts should be submitted on a single A4 sheet, accompanied by a mini-CV on a second A4 sheet. This should include your date of birth and up to five publications of relevance to the lecture topic. Please also supply the name, address and telephone number/email address of your head of department to assist in the selection process. Applications will be judged by the Awards Committee of the Society using the standard criteria of originality, scientific quality and general relevance/impact.

Send applications to Julie Cragg, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT **no later than 27 June 2003**.

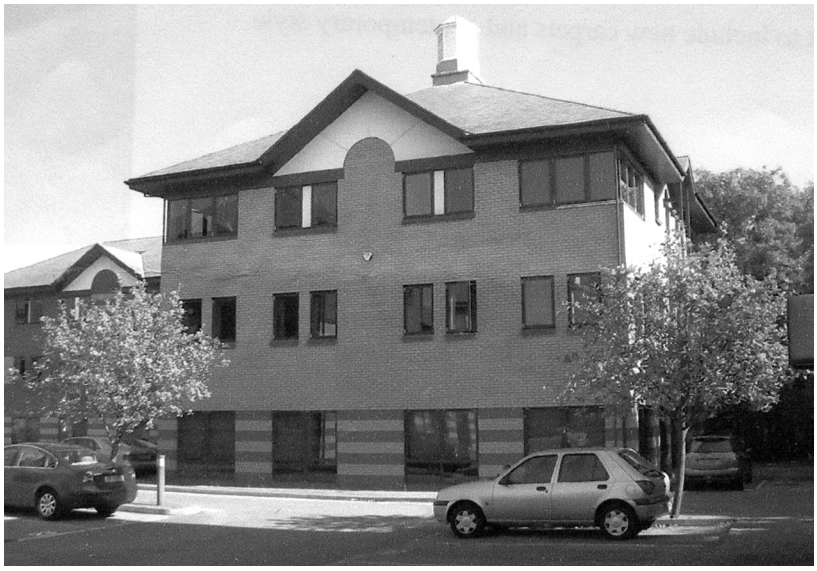
Clinical scientists are encouraged to apply for the Young Endocrinologists Clinical Review Lecture, held at the Clinical Cases Meeting each year in February.

Nominations for Council

Professors I A Hughes and J P Monson will retire from the Society's Council in November 2003. Ordinary Members are invited to submit nominations to fill these vacancies. Forms are included with this mailing and should be returned to the General Secretary at the Bristol office by **31 July 2003**. A ballot will be conducted amongst the membership if necessary, and the results will be announced at the 2003 AGM during the Society's annual meeting in London on 3-5 November.

Bigger and better!

From 16 May 2003, the Society should be contacted at its new offices: 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT. Our latest phone numbers and email addresses will remain the same (see page 2 of this issue), but make sure you don't use the following old numbers, which will cease to function: 01454-616046, 01454-619347, 01454-619036 and 01454-616071 (Fax).



2003 SUMMER SCHOOL

15-18 July 2003

Manchester University

Molecular Endocrinology Workshop

Advanced Endocrine Course

Clinical Practice Day

For details, see the training section at www.endocrinology.org, or contact Ann Lloyd in the Bristol office (ann.lloyd@endocrinology.org)

Grants are available to young endocrinologist members of the Society wishing to attend the Molecular Endocrinology Workshop

SOCIETY CALENDAR

15 July 2003
Molecular Endocrinology Workshop at Summer School
Manchester, UK

16-17 July 2003
Advanced Endocrine Course at Summer School
Manchester, UK

18 July 2003
Clinical Practice Day at Summer School
Manchester, UK

10-12 September 2003
Endocrine Nurses Training Course: The Pituitary Gland
Durham, UK

3-5 November 2003
194th Meeting of the Society for Endocrinology
London, UK

25 February 2004
Clinical Cases Meeting
London, UK

22-24 March 2004
BES 2004 (in association with EFES)
Brighton, UK

Call for medal nominations

Nominations are now requested for recipients of the following medals, which are awarded annually by the Society, in recognition of outstanding contributions to endocrinology. Nominations should be sent to Julie Cragg in the Bristol office by 7 July 2003. Nomination forms and a full list of previous medallists can be found under 'About the Society' at www.endocrinology.org, or from the office.

2004 Society Medal *(previously P J Lowry, I C A F Robinson, P M Stewart, S O'Rahilly, S Franks, J R Seckl, A J L Clark and J A Franklyn)*

2004 European Medal *(previously E Ghigo, I Huhtaneimi, B Vennström, J-Å Gustafsson, B Groner, E R de Kloet, G Schutz and H Gronemeyer)*

2004 Asia & Oceania Medal *(previously M J Waters, E R Simpson, I J Clarke, R Smith, J K Findlay, P D Gluckman, S Seino and J W Funder)*

2005 Dale Medal *(previously S R Bloom, D Baird, B McEwen, J Folkman, S Moncada, R P Ekins, H G Burger and M I New)*

2005 Transatlantic Medal *(previously K Parker, J R G Challis, B O'Malley, J M Friedman, D M Stocco, J F Strauss III, J C Marshall and D LeRoith)*

Members on the move...

B S Aditya to Broadgreen Hospital, Liverpool; M Badman to Hillingdon Hospital, Uxbridge; C Chandras to Harvard Medical School, Boston, MA, USA; R Fowkes to University of California, San Francisco, CA, USA; G MacColl to University of Edinburgh, Western General Hospital; A Melvin to Bedford Hospital NHS Trust: C T Musabayane to University of Durban-Westville, South Africa; N Papadopoulou to Tufts School of Medicine, Boston, MA, USA; C Parkinson to Ipswich Hospital; N Sarlis to University of Texas, Houston, TX, USA; B Zbytek to University of Tennessee, Memphis, TN, USA.

Peter Sonksen

We would like to extend our best wishes to Professor Peter Sonksen, a Senior Member of the Society, who was injured in a skiing accident earlier this year. Our thoughts are with Peter and his family.

With regret

We are sorry to announce the death of three members of the Society. Dr Sylvia Tait, of Brockenhurst, Hampshire, who was an Honorary Member, sadly passed away at the end of February 2003. Professor R C Wolf, a Senior Member, from Madison, WI, USA, and Dr Christopher Pearce from Ipswich both died in December 2002. Obituaries for Dr Tait and Professor Wolf will follow shortly.

OBITUARY

Keith Benson

The disparate worlds of veterinary science and autism lost one of their most ardent protagonists on Christmas Eve with the sudden death of Keith Benson. A zoology graduate of the University of Liverpool, Keith was a member of academic staff in the Faculty of Veterinary Science from 1961 until 1982. Previously, he had worked at the former National Institute for Research in Dairying in Reading, and had also spent a short sabbatical in Hong Kong. In 1964, Keith was a visiting professor to Cornell University in New York State. He was General Secretary of the Society for Endocrinology from 1971 to 1975.

After 25 years unravelling the mysteries of mammary gland physiology, he retired early in order to devote more time to autism, but he remained a strong supporter of the Society for Endocrinology and the Society for Reproduction and Fertility. Keith's commitment to autism was first formally recognised in 1963 when he became a Council member of the National Autistic Society (NAS). He was Chairman in 1975-1982 and again in 1989-1992. In 1990 he was awarded an OBE for services to autism, and since 1992 had been Senior Councillor of the NAS. With characteristic determination, Keith Benson quietly, but purposefully, revolutionised care for autistic adults throughout the UK. He was also instrumental in providing services for autistic children.

Keith paved the way for many diverse aspects of Care in the Community, both at a local and national level. In this work, he has been unerringly supported by his wife, Helen, daughter, Cathy and son, Neil - the inspiration for his devotion to autism. His other love was the Lake District, his spiritual home, where he so often walked the fells.

Donations in his memory may be made for the benefit of the Wirral Autistic Society, Raby Hall Road, Bromborough, Wirral CH63 0NN.

BES 2003

In March, the BES headed to Glasgow for its annual extravaganza of cutting edge endocrinology and social interaction. Here are just a few of the highlights.

Winners

The excellent abstracts submitted for the meeting led to some difficult decisions for the judges of this year's awards. We are pleased to congratulate all the winners, who were presented with their prizes during the BES Banquet. Thanks are especially due to our sponsors, who made these awards possible: the Michael White Memorial Fund, Novartis Pharmaceuticals UK Ltd and Pharmacia.

Niamh Martin receiving her Novartis Award

This year's Michael White Memorial Prize was won by Karin Bradley, for her abstract 'Parafibromin germline mutations in patients with parathyroid tumours'. This £500 award recognised the best oral communication from a young endocrinologist regarding clinical or basic research in the field of endocrine neoplasia. This was the fourth, and last, in a series of prizes in memory of the late Professor Michael White, who was an active and respected member of the Society for Endocrinology.

Two abstracts were selected for the 2003 Novartis Awards, which were awarded for the best submissions by young endocrinologists. Niamh Martin and F Fisher each won an £1000 prize for their respective abstracts entitled 'Abnormalities of thyroid function in the POMC-null mouse' and 'Expression of adiponectin protein in human fat: the effect of type 2 diabetes and obesity'.

Last, but not least, this year's British Endocrine Societies Awards supported by Pharmacia was won by Wendy Clarke for her study 'Inducing pancreatic b-cell regeneration: interactions of transcription factors and peptide growth factors'. This major £10,000 research grant is awarded for clinical and basic science laboratory research proposals in the field of endocrine growth factors, and will contribute towards Wendy's ongoing research at the Department of Medicine in the University of Birmingham.

In addition, six travel awards of £500 were awarded to Zubair Ahmed (Neuronal delivery of short interfering RNA (siRNA) to knockdown growth inhibitory pathways and improve growth factor-stimulated axonal regeneration in the injured CNS), Lee Barrett (Delivery of a neurotrophic growth factor to CNS neurones self-replicating RNA), Duncan Bassett (Familial isolated primary hyperparathyroidism due to germline multiple endocrine neoplasia type 1 mutations), Andrew Bicknell (Characterisation of the adrenal mitogen), Catherine Lagord (Preservation of spared axons following spinal cord injury by delivery of key angiogenic growth factors) and Claire Stewart (Interaction of soluble and biophysical cues in skeletal muscle maintenance).

Anyone for tennis?

Those of you disappointed by the postponement of the tennis tournament at the BES meeting may be pleased to hear that it will now take place during the Endocrine Society meeting in Philadelphia on 19-22 June 2003. Please register your interest in advance by contacting Maggie Carson on m.n.carson@ed.ac.uk. Our thanks go to Pharmacia for sponsoring the event and for providing magnificent glass trophies, which will be presented to the winning doubles partnership.

Nurse news

BES 2003 saw a suite of sessions dedicated to nurses. Sarah Frewin ran the second interactive workshop on patient group direction (PGD). After a short presentation, the 23 nurses who attended worked in small groups to develop PGD for the modification of various medications. The aim was to give delegates an idea of how to tackle this in their own place of work. If you attended this session and would like a copy of the overheads, please contact Tamara Lloyd in the Bristol office.

The nurse symposium 'Ethical dilemmas' attracted 53 delegates from both the medical and nursing professions. Professor Sir John Lillyman discussed the issues surrounding consent, and this was followed by presentations from Karen Campbell and Margaret Miller. (We are very grateful to Margaret for kindly stepping in at the last minute to replace our original speaker Jim Smith, who, as a serving member of the TA, had very recently been called up).

Finally, thanks are again due to Serono for sponsorship of the nurses tea, which gave members a chance to meet and compare notes between sessions.

MAGGIE CARSON

Now turn to the back cover for a further insight into BES activities...

Webspinning

Melissa Westwood highlights the best on the web

Macromolecular museum

www.callutheran.edu/biodev/omm/gallery.htm

This is a site for the display and study of macromolecules, and thus the authors rightly designate their collection as a museum. Although under construction, the 'halls' currently exhibit the essential 'molecules of life' - DNA and amino acids - as well as the structure of molecules involved in DNA modification/repair, membrane biology, cell adhesion, immunology and virology. A frames-compatible browser and a Chime plug-in (free download) are required to view the structures, as part of an interactive, animated tutorial on their important biochemical features. Definitely worth a look, if only to marvel at the advances in structural analysis.

SERVICES: L, O (images); STRONG POINTS: Images; WEAK POINTS: Nothing significant; RATING: Very good.

Human genome variation

www.hgvs.org

Following on from mouse mutaneering (see last issue), here's a site that focuses on human mutations. It's maintained by the Human Genome Variation Society, which aims to 'foster discovery and characterisation of genomic variations' by enabling the collection, documentation and free distribution of information relating to human mutations and their phenotypic consequences. Several aspects of the site are unremarkable (meeting information, newsletters etc.). However, the links to mutation-based databases and educational pages are excellent, and many will welcome their recommendations for mutation nomenclature.

SERVICES: N, L; STRONG POINTS: Links; WEAK POINTS: None; RATING: Good.

Endocrine disrupters

europa.eu.int/comm./environment/endocrine

Buried amongst the pages of Europa - the European Union On-Line - this site on endocrine disrupters opens with sections on 'What is the endocrine system?' and 'Why its important for life', and so may be more appropriate for the public than the Society's membership. However, it nicely summarises disrupters' mechanisms of action and their known biological effects, and provides detailed information on the European Commission's strategy for dealing with this issue, as well as global initiatives.

SERVICES: N, L; STRONG POINTS: Educational content; WEAK POINTS: Too basic for endocrine researchers? RATING: Good.

Thanks to Kevin Ahern and *Genetic Engineering News*. Don't forget to visit the Society for Endocrinology on the web: www.endocrinology.org; tell us about your favourite web site: melissa.westwood@man.ac.uk

KEY **Services** provided at web sites:

- **T** Tools - Analytical computing tools
- **D** Data - Searchable or downloadable database information
- **G** Goods - FTP delivery of useful items (e.g. full package, bug fix or demo software)
- **L** Links - Useful links to other sites
- **N** News - News of interest
- **S** Support - Feedback in response to users' enquiries
- **O** Others - e.g. Innovative use of web tools, appearance, editorial point of view

Ratings: Excellent, Very Good, Good

Nothing below good will be reported here.

Clinical Endocrinology Trust grants

Ten awards of £1000 are available from the Clinical Endocrinology Trust. The awards will enable undergraduate medical students to undertake a project of up to 3 months' duration on any aspect of endocrinology.

Research will normally take place in the UK under the guidance of a supervisor, and the money provided will be expected to cover laboratory and other expenses. A 500-word report must be submitted to the Trustees on completion, and an abstract may be submitted to a future BES meeting. The Trustees will award a further £1000 for the best report. Applications should include an outline of the project (on one sheet of A4 paper), a sponsoring letter from the prospective supervisor, a CV and estimated expenses. They should be sent to Julie Cragg at the Society for Endocrinology's Bristol office by 31 July 2003.

HypoCCS Award 2004

Achievement in the field of hypothalamus-pituitary diseases and their impact on peripheral receptive tissues or organs will be recognised by this $20,000 award, sponsored by Eli Lilly and Company. It will be presented at the HypoCCS Symposium in San Antonio, Texas, USA on 10-13 March 2004. The recipient will be invited to give a lecture and submit a manuscript for publication in the symposium's proceedings.

Nominations should comprise: a statement of up to 1000 words, outlining the candidate's research achievements during the last 5 years, their CV (with bibliography), and a list of their ten most important publications, demonstrating their contribution to advancement of the field.

Studies in either clinical or basic science at an academic institution are eligible. Nominees should be less than 45 years old at 31 December 2003. Self-nominations will not be accepted.

Nominations must be submitted by 15 October 2003. They should be emailed to pierre.c.sizonenko@hin.ch, and also forwarded to Pierre C Sizonenko, 17 rue Toepffer, CH-1206 Geneva, Switzerland (Fax: +41-22-3471734).

HypoCCS winner

Congratulations to Kris Chatterjee of Addenbrooke's Hospital who been awarded the seventh HypoCCS Award for his group's studies into the genetic basis of endocrine disorders.

Delving into data

Even before the Domesday book, man was collecting and analysing data in order to describe his condition. The advent of the computer brought the ability to design and operate databases within the grasp of every clinical scientist.

We can all appreciate the importance of large epidemiological studies of diseases and their treatment in guiding and informing research. For example, the hypothesis that the increased mortality in hypopituitarism is due to growth hormone deficiency was generated by studying mortality in a cohort of patients who had undergone surgery for pituitary tumours. The challenge, however, is to define the rules required to gather, process, fund and interpret the massive volume of data that is now being collected in national and international databases.

In this themed issue, we have asked representatives from the management boards of four data-collecting projects to give us some insight into the structure of their studies. KIMS and HypoCCS are both international operations with international boards, yearly meetings and budgets that must exceed millions of pounds, whereas CaHASE and the UK National Acromegaly Database are national operations run on relatively small budgets through the Society for Endocrinology. We are lucky to have received four excellent articles, and hope that they will stimulate a debate within the Society on how to develop and manage the clinical databases of the future.

RICHARD ROSS

CaHASE: CAH beyond childhood

Congenital adrenal hyperplasia (CAH) can be a very distressing disease. Parents whose children are diagnosed at birth may have to come to terms with both their need for lifelong steroid treatment and, in females, the issues associated with ambiguous genitalia. CAH is characterised by a defect in one of the enzymes required for adrenal cortisol biosynthesisis (usually 21-hydroxylase). There are varying severities of the disease, depending on the actual genetic defect inherited.

Most of the current literature on CAH concentrates on the disease in childhood. To try to redress this imbalance, the Society for Endocrinology recently conducted an audit of adults with CAH in the UK. This audit revealed a lack of consensus on methods of treatment and monitoring for adults with CAH (see *Journal of Endocrinology* 2000 **164** Suppl S38). There is a need for further research to improve treatment of these patients and thus their physical and psychological well-being.

Seven of the UK's leading endocrinologists have therefore come together to form CaHASE (or the Congenital Adrenal Hyperplasia Adult Study Executive). Its remit is to specifically address CAH in adult patients. The current members are John Connell (Glasgow), Gerry Conway (London), Ashley Grossman (London), Richard Ross (Sheffield), Paul Stewart (Birmingham), Helen Turner (Oxford) and Brian Walker (Edinburgh). In the future CaHASE hopes to recruit new centres to make the project a truly UK-wide initiative.

CaHASE has now set up a multi-centre prospective study, to enable collection of informative data by investigating a suitably large cohort of UK adults with CAH. The aim is to gather information on a range of clinical indices (treatment, body composition, biochemical analysis including lipid profiles and fasting insulin, and fertility), as well as the psychological/quality of life issues that affect adults with all forms of CAH (classical and non-classical, salt-wasting and non-salt-wasting, and all genotypes). The ultimate objective is to generate original research that will help to inform the day-to-day management of adults with CAH.

DEBBIE WILLIS
CaHASE PROJECT MANAGER

CaHASE are very grateful to the Clinical Endocrinology Trust, who have supplied a grant for this project. Melissa Hines' article on page 11 addresses further issues associated with CAH

HypoCCS: GH replacement in adults

Treatment of adults with growth hormone deficiency (GHD) is very different from treatment in childhood. Experience with adult GHD is limited (the indication was registered in Europe only in 1995), and results cannot be extrapolated from children. For this reason, Eli Lilly and Company committed to a long-term observational study, the Hypopituitary Control and Complication Study (HypoCCS).

The objectives of observational studies include monitoring of safety under routine clinical conditions (including modalities which can influence drug efficacy and safety like indication, dosage, duration and interaction with other treatments); investigation of special risk groups (the elderly, co-morbidity); and assessment of the effect of treatment on outcomes (clinical, quality of life, economic).

continued on page 8

HypoCCS: GH replacement in adults

continued from page 7

These criteria could obviously apply to a study of adult GH replacement. Indeed, adult GHD observational studies have already contributed significantly to optimising treatment, including improved diagnostic and dosing algorithms, and the ongoing assessment of the efficacy and safety profile. However, adult GHD treatment, like almost all endocrine treatments, means lifelong replacement. So, based on our current knowledge of adult GHD and hypopituitary disease, the risks associated with the underlying disease and the cautions regarding therapy, the relevant questions can be specifically reformulated as follows.

1. Does long-term GH replacement have any effect on the incidence of any tumour type?
2. What are the long-term clinical benefits of GH replacement in terms of cardio-/cerebrovascular outcomes, quality of life, fracture incidence, and overall patient care?

Patients' data have been collected into the HypoCCS database since 1996, with patients from registration studies having been on drug exposure since 1991. The HypoCCS International Advisory Board (the experts who govern HypoCCS) soon recognised that the success of the study would be based on its ability to answer the above questions. This implies huge challenges, some of which are discussed here.

In observational studies, assessments are generally performed on person-years available in the database at a given time point. Whatever the study design, this approach may provide statistically significant results. However, the power may be significantly reduced if a prospective sample size calculation is not in place. This would bias the value of any assessment made, for example, on tumour incidence or cardiovascular outcomes under GH treatment. This was recognised in the HypoCCS protocols that were initially implemented separately in Europe and USA. Consequently, it was decided to merge the databases into a single protocol, where prospective power calculations are provided for two analytical approaches.

1. Comparison of the GH-treated cohort with a non-randomised group of GH-untreated patients. Non-randomisation creates potential bias, but differences between treatment groups can be balanced using appropriate statistical methodology (propensity score).
2. Comparison of outcomes of GH-treated patients with normal population references. Risk estimates for a given outcome are calculated from incidence rates in a normal reference population.

The HypoCCS study description provides details of sample size calculations for different outcomes using the two analytical approaches. In brief, 8000 patients will be required to detect a 50% increase in non-CNS cancer and a 33% decrease in cardiovascular complications using the first approach. With the second, assuming the database size remains constant, a follow-up until 2005 will be required to confirm a standard incidence ratio (SIR) of 1.25 for all malignant neoplasms, and of 1.5 for cardiovascular diseases. An SIR of 1.5 will indicate a significant effect of GH treatment, as GH-untreated patients have an SIR twice that of the normal population.

The scenarios created by these calculations are important, because they clearly indicate the patient numbers and the observation time required to provide reliable answers in terms of long-term safety and efficacy of GH replacement in adults.

So, at least 8000 patients need to be followed for several years in order to be able to assess long-term outcomes in HypoCCS. Over 5000 patients have enrolled in the study, and data from over 21,000 patient visits have been collected. This amounts to over 10,000 patient-years experience, but, as outlined above, it is clear that the follow-up time now needs to be increased to properly evaluate safety outcomes. The mean duration of follow-up is currently just over 2 years, but sufficient numbers exist to provide analysis of some variables up to at least 4 years. Such a large sample size generates major logistical challenges.

Given the observational nature of the study, the most critical (and resource-consuming) aspect is to ensure the quality of the collected data. Adverse events in particular are scrutinised for completeness and consistency and, where necessary, sites queried as they would be in a clinical trial, but without source data verification. Internally, we also conduct cross-validation checks with our pharmacovigilance database. With the advent of electronic data entry systems, we expect this laborious process to become streamlined, and for it to be possible to maintain high data quality even in an observational setting over many years. The provision of central laboratory services and quality of life instruments developed for hypopituitary patients improves the consistency of data used in outcomes analysis. For a multi-centre study like HypoCCS, it is necessary to use a robust data management process of the type available in pharmaceutical companies or in contract research organisations. This provides an audit trail and an infrastructure that allows access to the data in the appropriate format for analysis.

An advisory board reviews the data and makes recommendations for further analyses or changes to the data collection or analysis process. This group is charged with publication of periodic reports. Increasingly, bodies concerned with outcomes, like NICE in the UK, expect to be able to review such data, and thus HypoCCS data were made available to NICE during its recent appraisal of adult GH replacement. The results of annual reviews provide feedback for contributing physicians and regulatory bodies, as well as a means of checking whether results fit current scientific opinion.

Resourcing requirements change as the study develops, but support is needed for: study set up and developments; site management (training, advice etc.); laboratory services; data collection, management (entry, queries, quality assurance etc.) and analysis; scientific steering committee for periodic result analysis; publications and reports; advisory board and consultants.

Studies like HypoCCS can provide valuable data sampled from the full spectrum of patients and outcomes. These compliment data obtained in clinical trials, where the patient population is carefully selected. By comparing outcomes of treated patients with those of untreated groups, or with population norms, it is possible to increase the knowledge base that underpins our clinical practices significantly.

A F ATTANASIO, D J EDWARDS
ELI LILLY AND COMPANY

UK National Acromegaly Database

Established in 1997, this database was set up by a group of interested endocrinologists, after a successful pilot in Edinburgh. Its aim is to obtain sufficient data from UK patients with acromegaly to enable statistically sound epidemiological data to be derived. It will allow the effects of the complications and treatment of acromegaly to be individually assessed in terms of the known increase in morbidity and mortality in untreated patients.

Any UK endocrine centre involved in the management of acromegaly can participate, and several small centres are now involved, even though the initial focus was on those with more than 40 patients. The 1664 records that have been entered by 18 centres across the UK represent approximately 66% of the total number of acromegalic patients (2520) at these centres. A further 550 patients have been identified at eight new centres that are in the process of starting to enter data.

Each contributing centre maintains a local database file. Detailed retrospective and prospective clinical data are entered and validated according to defined criteria. Data field definitions are specified by a Steering Group drawn from the contributing centres. A defined anonymised subset of the full local dataset for each patient is submitted at 3-monthly intervals, to be merged with the national database file. Algorithms built into the database software perform internal data validation. The software, based on tables in Microsoft Access®, is designed to recognise a broad range of apparent internal data inconsistencies and omissions; these are logged to a table for cross-checking. External data validation is performed on a subset of records by both the national data co-ordinator and the local consultant, who cross-check database records against clinical notes. This structure enables consistent validated data to be collected from across the UK. A major upgrade to the database is planned. This will provide a greater degree of flexibility, and enable adaptation for similar conditions.

Maintaining motivation among those involved in the project is important. In addition to on-site visits for initial training and subsequent support, regular training days are organised by the national co-ordinator, to which all staff who enter data (usually the local endocrine specialist nurses) are invited. This ensures that data entry is well understood. Topics covered include data entry and validation, data queries, feedback from national and international meetings where data has been presented, target setting, assessment of the current status of the project, and other topics requested by those attending.

Several technical issues have had to be resolved. Not every centre has had access to a computer with the appropriate specifications. In many centres, computers are shared between several members of staff, creating problems of access for those entering data. The ongoing evolution of the database programme has also necessitated extensive piloting of software upgrades.

Personnel issues have included the need for staff to familiarise themselves with both the database and the many software upgrades. Most of the staff involved in data entry are working alone on this project and this can be isolating. Furthermore, staff working part-time or on short-term contracts have left for more stable employment, necessitating the search for a replacement and time to retrain. This has meant periods where data entry was at a standstill at several centres. This can quickly lead to data becoming out of date.

Searching through medical notes and transferring information to the database is extremely time-consuming. Recent analysis has shown that it takes about an hour to enter data regarding a newly diagnosed acromegalic, and between 2 and 4 hours for a patient with a long history.

Ethical issues are important and previously local consent was obtained. We are now applying for MREC approval and patient consent is mandatory. There is a new consent form and patient information sheet.

Whilst initially supported by the Department of Health, the project has also been supported by an unrestricted educational grant form Novartis (UK/Germany) to enable the database to be rewritten, and for this we are very grateful. Funding has allowed payment of the project co-ordinator, training, and a small payment to centres for each complete historic record accepted.

Maggie Carson, National Co-ordinator

We have presented several abstracts at meetings in the UK and USA. It is important to involve all the people involved in data gathering, and adequate time must be devoted to getting feedback from these abstracts. We have produced three papers, which are almost ready for submission: one on radiotherapy, one on medical therapy, and one on the effects of surgical treatment. These show that radiotherapy is effective in the largest cohort of patients reported thus far. They also show, again in the largest cohort of patients reported, that medical treatment with somatostatin analogues is effective, but pre-treatment growth hormone is of key importance in predicting the proportion of patients that will respond. The surgical data are more controversial, and show wide-ranging differences in surgical outcomes across the UK.

Our acromegaly database has required an enormous amount of energy from a large number of people to establish and maintain, and finance has often been a concern. However, the end result will be a number of seminal papers on the treatment of acromegaly. Hopefully, in the next few years, data will emerge which show the various risk factors that improve or worsen the mortality and morbidity of the disease.

MAGGIE CARSON, SUE THORN
PETER BATES, JOHN WASS

A copy of the dictionary of data field definitions is available from Maggie Carson (National Co-ordinator; Email: m.n.carson@ed.ac.uk). Further information on the database redevelopment is available from Jonathan Seagrave (Project Support Officer; Email: jon.seagrave@endocrinology.org)

KIMS: treating adult GH deficiency

Some 14 years have passed since the publication of the first placebo-controlled trials examining the treatment of hypopituitary adults with growth hormone-deficiency (GHD) by replacement of GH. Since then, the vast array of published material has largely confirmed the original observations, despite progressive reduction in the doses of GH used.

Specifically, there has been increasing recognition of a clinical syndrome of adult GHD. This is characterised by abnormal body composition, with increased central fat and decreased lean body mass, and the variable presence of unfavourable lipoprotein profiles, increased predisposition to atherogenesis, decreased energy levels and psychological well-being, decreased bone mineral density and a possible increase in cardiovascular morbidity and mortality. The beneficial effects of GH replacement on these clinical features has been demonstrated repeatedly in subsequent placebo-controlled and longer-term open studies. Observations have also confirmed an increase in the standardised mortality ratio (SMR) in hypopituitary adults treated with conventional replacement, excluding GH.

The precise cause of the increased mortality in hypopituitary adults remains unclear, and is likely to be multifactorial. However, the presence of unfavourable changes in cardiovascular risk factors in the hypopituitary GHD adult, and their reversal with GH replacement, provides surrogate evidence for an aetiological contribution from GHD. Against this background, in 1996, GH was licensed in the UK for use in GHD adults who fulfilled specific criteria, including the presence of structural pituitary disease and/or the presence of additional pituitary hormone deficits.

KIMS (originally the Kabi International Metabolic Study) is an international metabolic database and pharmacoepidemiological survey of adult patients with GHD receiving recombinant human GH replacement, and is sponsored by Pharmacia Corporation. The KIMS database was designed in anticipation of the use of GH replacement in clinical practice and, following ethical approval, the first patient was enrolled in 1994. KIMS was modelled on the highly successful KIGS paediatric database, which has provided a vast quantity of longitudinal information on the use of GH replacement in paediatric growth disorders.

The primary aims of the KIMS database were to monitor long-term safety during GH replacement, to provide observational data to facilitate its optimisation, to document baseline characteristics and response to therapy among patients who were divided into small subgroups in individual clinics, and to monitor mortality rates. It was originally anticipated that more than 5000 patients would need to be followed for at least 5 years. KIMS has since enrolled over 8000 patients from 26 countries, and active recruitment continues. Currently, the UK is the largest single contributor, with over 1800 patients enrolled (approximately 80% of all adult patients treated with GH in the UK).

Following enrolment, patients are seen in their local clinics at least once a year, at a frequency determined by the treating physician. At each visit, clinical information is recorded on specific case record forms. Quality of life (disease-sensitive questionnaires) and socio-economic factors are also recorded. Data collection and recording are monitored by clinical research representatives of the sponsoring company, according to good clinical practice guidelines, and anonymised information is entered into the central database. Serum IGF-I and lipid measurements are performed annually on all patients in a central laboratory.

The accuracy of data entry into the database is subject to internal audit and is scrutinised by the physician members of a strategic scientific committee, who also have responsibility for commissioning specific data analyses to address various treatment outcomes and safety issues. Data analysis and publication are performed by appointed project units, consisting of experts in the area in question, supported by a member of the strategic committee, with statistical support provided by the sponsoring company.

The governance of the database is recorded in legally binding statute, such that the ultimate ownership of the data remains with the contributing physicians. Elected national boards are responsible for issues within individual countries. Each sends at least one representative to the KIMS International Board, which is the ultimate decision-making body. By virtue of this organisational structure, KIMS has remained a physician-managed database, whilst benefiting from major financial and logistical support from industry.

So what has KIMS contributed during its operation? It has confirmed that, thus far, GH replacement is not associated with an increased risk of de novo neoplasia or diabetes mellitus. It has provided the single largest description of baseline clinical characteristics of hypopituitary adults, confirmed an increased risk of fracture in older hypopituitary adults compared with age-matched control populations, documented among the first indications of the important gender differences in susceptibility to GHD, and delivered a rationale for the use of GH dose titration against serum IGF-I, which has now become standard practice.

KIMS has also quantified improvements in the utilisation of health care resources in patients receiving GH replacement, and documented beneficial effects of GH replacement in minority subgroups of patients, including hypopituitary adults aged over 65 years and those treated previously for acromegaly or Cushing's disease. Reassuringly, the analyses of mortality rates in KIMS, which are performed on an annual basis, continue to demonstrate SMRs which are indistinguishable from country-adjusted background rates, in contrast to the increased SMRs demonstrated in epidemiological studies of hypopituitary GHD adults.

The value of KIMS and its relevance to everyday clinical practice was clearly demonstrated during the recent evaluation of the adult GH indication by NICE, in which KIMS data provided the sole basis for the health economic analysis. Whilst the randomised placebo-controlled clinical trial remains the gold standard for proof of concept, KIMS has clearly demonstrated the value of outcomes research databases in documenting the real-life, long-term benefit of specific therapeutic interventions, and in strengthening our evidence base.

JOHN P MONSON
CHAIRMAN, UK KIMS NATIONAL ADVISORY BOARD, MEMBER OF KIMS STRATEGIC SCIENTIFIC COMMITTEE

Professor Monson thanks Dr Patrick Wilton, Dr Maria Koltowska-Häggstrom and the Pharmacia team, his colleagues on the KIMS Strategic Scientific Committee and International Board, and the KIMS Investigators worldwide for their support of this project.

Boys will be boys...?

Melissa Hines examines the current evidence for the lifelong influence of prenatal androgen on brain and behaviour.

Beginning almost as early as life itself, the mammalian brain is a primary target for gonadal steroids. The fetal testes are active by week 8 of gestation. Their products influence basic processes of neural development, including cell death and survival, neuroanatomical connectivity, and neurochemical specification in brain regions containing hormone receptors. As a result, prenatal alterations in gonadal steroids can have permanent behavioural consequences.

The importance of testicular hormones for neural and behavioural development has been established in experiments with non-human mammals. For example, treating genetically female (XX) rats with a single injection of testosterone on their day of birth permanently alters their sexual behaviour, producing female animals with male-typical rather than female-typical reproductive behaviour in adulthood.

Other behaviours that show sex differences are also influenced by manipulation of the early hormone environment. In rodents, testicular hormones affect rough-and-tumble play, scent marking, feeding and body weight regulation, and physical aggression. The influences of hormones are not limited to rodents, but are seen in virtually all mammals, including non-human primates. For example, the female offspring of rhesus monkeys treated with testosterone during pregnancy show increased rough-and-tumble play as juveniles, and increased masculine sexual behaviour and reduced feminine sexual behaviour as adults.

The behavioural changes caused by early hormonal manipulations are accompanied by dramatic alterations in brain structure. Cell groups in a number of regions of the rodent brain that concentrate high levels of gonadal steroids are several-fold different in volume in male versus female animals. In females that have been treated with testosterone during early development, these brain regions look like those of males.

Do gonadal steroids exert similar influences on human brain development and human behaviour? Experimental manipulation of hormones during early development is generally unethical in humans. However, some relevant information comes from studying individuals with intersex conditions, where a prenatal hormonal abnormality has caused genital ambiguity at birth.

The most common cause of genital ambiguity at birth is congenital adrenal hyperplasia (CAH). Girls with CAH are born with various degrees of genital virilisation, involving clitoral enlargement and labial fusion. Typically, they are surgically feminised in infancy, treated with hormones to regulate their condition postnatally, and reared as girls.

However, the behaviour of girls with CAH differs in some respect from that of other girls. Most notably, they show masculinised play behaviour, manifested in increased preferences for toys usually chosen by boys and for male playmates, and reduced preferences for toys usually chosen by girls. Females with CAH also are somewhat more likely than other women to report bisexual or homosexual erotic interests. However, although the incidence of same-sex attraction is increased in women with CAH, the majority report a heterosexual orientation.

In addition, XX individuals with CAH who have been reared as girls are almost always typically feminine with regard to the most fundamental aspect of psychosexual development, that of core gender identity or the sense of self as male or female. However, the incidence of atypical identity, or gender dysphoria, although rare, is higher than would be expected in the population at large. In those rare cases where XX individuals with CAH have been reared as boys, they generally evolve a male core gender identity.

Some genetic males who have been born with genital abnormalities have been reared as females. Such abnormalities are typically caused by reduced testicular androgen levels or reduced sensitivity to androgen, such as occurs in androgen insensitivity syndrome. In some cases, even XY individuals with apparently normal androgen levels prenatally have been assigned and reared as girls. This may occur, for instance, if a child is born with testes, but no penis, or with other disorders that prevent normal penile development, despite the presence of testes.

In even more extreme cases, genetic males, born without genital ambiguity, have been reassigned as female following damage to the penis during infancy. In one such case, the damage occurred at 7 months of age and, although reassignment as a female was reportedly successful in childhood, the individual subsequently chose to live as a man and reported having experienced gender dysphoria for many years. He also married a woman and indicated that his sexual orientation was that of a heterosexual male. This case has been widely publicised, and has led to suggestions that exposure of the brain to male-typical levels of testicular androgens prenatally precludes development of a female gender identity.

However, in another well-studied case, a male infant was reassigned as female following penile damage at the age of 2 months, and the outcome was different. At the ages of 16 and 26 years, this individual's core gender identity was female, and her sexual orientation was bisexual. Similarly, although there is an occasional report that XY individuals with intersex conditions develop gender dysphoria when reared as females, most such individuals evolve a female identity, although, like women with CAH, they are more likely to be bisexual or lesbian than are other women.

So it appears that prenatal exposure to high levels of androgens pushes psychosexual development in the masculine direction, at least as regards childhood play behaviour and sexual orientation. Despite these hormonal influences, however, human beings appear to be surprisingly flexible with regard to core gender identity. This is not to say that outcomes are perfect for individuals with intersex conditions, regardless of which sex is assigned. Although many individuals, even those with a Y chromosome and exposure to a male-typical hormone environment prenatally, evolve a female gender identity, some do not.

The causes of this variability in outcomes are of great interest. Possibilities include the amount of social and psychological support that is available to the individual, the ability of the parents to view the child unambiguously as a person of the assigned sex, the age at which the sex assignment occurs, and even the conviction of the attending physicians and other clinicians that the assignment will succeed.

MELISSA HINES

Doctors and Patients: An Anthology

Ed C Holman, Radcliffe Medical Press, 2002, 176 pp, £19.95, ISBN 1 85775 993

This anthology comprises sixteen short stories by famous and not so famous literary figures, focusing on the doctor-patient relationship from three perspectives: doctors, patients who have experienced a serious life-threatening disease, and clinical encounters.

Ten of the sixteen authors were or are actually physician-writers, the better known being Sacks, Maugham, Conan Doyle, Cronin, Williams, Bulgakov and Chekhov. In each case, the fact that the authors are or were doctors themselves gives their narratives a particular quality of authenticity. After all, authors of fiction are most convincing when writing in fields they know or have experienced.

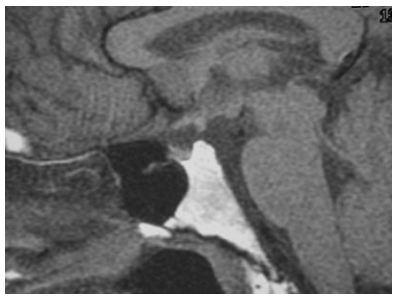
In truth, there is no specific endocrine flavour to any of the stories. To some extent this is very understandable, as the context for the majority is a life-threatening disease, such as cancer, or infectious diseases that were more prevalent and dangerous in the past. In contrast, endocrinology is primarily a quality of life discipline. Acute risk of death from an endocrine disorder (other than diabetes mellitus) is a reality, but it is not commonplace. Emergency call-outs for an acute case of short stature, delayed puberty or overnight infertility do not occur!

Nonetheless, one consequence of the chronic nature of endocrine practice means that longstanding relationships are established with patients who return year after year. As a result, it remains incumbent upon its practitioners to continue to understand the impact of the patient's disease on his/her life. Endocrinologists' greatest vulnerability lies in their capacity to sacrifice an interest in their patients' lives for an obsession with biochemical numbers. If you think you might have fallen into this habit and regret it, then pick up this book and reflect.

S M SHALET

Erratum

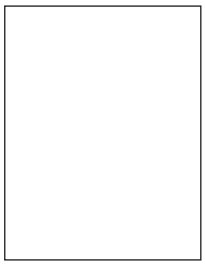
Apologies to Jane Evanson, author of 'The forgotten lobe', on page 10 of the last issue. Unfortunately, the figure that was printed was incorrect, and showed a large hypothalamic hamartoma arising from the tuber cinereum in a patient with precocious puberty. The correct figure (shown here) depicts a sagittal T1-weighted MR image demonstrating the absence of the pituitary stalk with an ectopic posterior pituitary lobe lying at the level of the median eminence, as described in the caption.



Hot Topics

The pick of the latest research from the Society's journals, brought to you by Nathalie Gilmore, Jolene Guy and Mona Munonyara

Epithelial action of FGF7 in breast cancer



Fibroblast growth factor 7 (FGF7) is a potent growth factor for mammary cells, but its origin, cellular targets and actions have been unclear. In this study, Palmieri and colleagues address these issues, and discuss the implications for human breast cancer research.

Using specific antibody immunostaining, FGF7 and FGF10 have been localised in epithelial and myoepithelial tissue of normal breast and breast carcinoma sections. This indicates that localisation is due to receptor binding, and confirms that, despite evidence for a stromal origin of FGF7, its receptors are not found in stromal cells. Thus, the cellular targets of FGF7 in the breast appear to be epithelial cells, not fibroblasts. In contrast to previous studies on FGF7 as a mediator of hormonal action, interleukin-b, rather than oestrogen receptor ligands, caused a dose-related release of FGF7.

As the first to demonstrate a mitogenic effect of FGF7 on both epithelial and myoepithelial breast cells, this study provides an interesting and valuable contribution to our understanding of the potential role of FGF-7 in breast development and breast cancer. JG

(See the full article in Journal of Endocrinology 177(1), April 2003)

Biological clock ticks for hypertension?

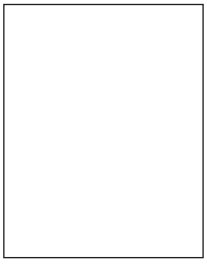
Physiological functions and activities of most organisms run on the 24-hour cycle determined by sunrise and sunset. In mammals, the suprachiasmic nucleus (SCN) of the hypothalamus is the master clock that regulates circadian rhythms. In this review, Bujis and coworkers discuss possible mechanisms whereby the SCN communicates these rhythms to the rest of the body.

The axis between the SCN and the paraventricular nucleus (also in the hypothalamus) is crucial for the organisation of neuroendocrine and autonomic mechanisms that control hormone secretion. Via this axis, the SCN synchronises the sensitivity of the target organs to match hormonal peaks.

The authors postulate that desynchronisation caused by pathology of the SCN might form the basis of chronic diseases such as hypertension. They report postmortem pathological changes in the SCN of hypertensive subjects. This intriguing finding indicates that changes in the SCN might be a cause or consequence of hypertension. MM

(See the full article in Journal of Endocrinology 177(1), April 2003)

Targetted activation of MAP kinase



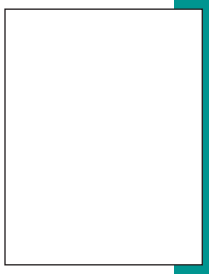
G protein-coupled receptors (GPCRs) form the largest superfamily of cell surface receptors in the human genome, and come in a diverse range of sizes and complexities. This diversity allows for a high degree of specificity, and this timely review by Lutrell reviews the many different ways in which MAP kinase activity can be affected by the GPCRs.

Using the example of the kinase 1 and 2 cascade regulated by extracellular signals, the author summarises the complexity of networks through which MAP kinase activation can occur. He discusses the roles played by different families of G proteins, as well as the influence of scaffolding proteins, which make these reactions more efficient and prevent cross-talk.

Depending on the cell type and cellular context, different combinations of these scaffolding and G proteins come together and, through the GPCRs, cause the specific activation of spatially localised pools of MAP kinase, thus ultimately determining their function. NG

(See the full article in Journal of Molecular Endocrinology 30(2), April 2003)

Prostate cancer: the genetic challenge



In the USA, one in eight men will develop prostate cancer during their lifetime. Family studies indicate a strong genetic influence, but there have been problems determining the genetic basis for this malignancy. This definitive review by Simard and colleagues summarises the current knowledge gained by studying the pedigrees of families affected by prostate cancer.

They discuss the three genes which have been identified as strong candidates for determining susceptibility, namely ELAC2, RNASEL and MSR1. In addition, they consider genes which, as moderate-risk variants, may contribute to this disease, for example, BRCA 1 and (more especially) BRCA 2, as well as common allelic variants of gene products involved in androgen biosynthesis and action.

The authors conclude that, due to the heterogeneity of prostate cancer, future studies must use larger cohorts of prostate cancer samples, comparing them with ethnically matched controls. They anticipate that data obtained from these studies, used in conjunction with other methods such as functional genomics, quantitative proteomics and bioinformatics, may help to discriminate between hereditary and sporadic prostate cancer cases, and will result in a dramatic increase in our understanding of this disease in the future. NG

(See the full article in Endocrine-Related Cancer 10(2), June 2003)

ENDO 2003: 85th Annual Meeting

Philadelphia, PA, USA, 19-22 June 2003.

Contact: Beverly Glover, Administrative Assistant, Meetings, The Endocrine Society, 4350 East West Highway, Suite 500, Bethesda, MD 20814-4410, USA (Tel: +1-301-9410220; Fax: +1-301-9410259; Email: bglover@endo-society.org; Web: www.endo-society.org).

4th International Symposium on Hormonal Carcinogenesis

Valencia, Spain, 21-25 June 2003.

Contact: Tandria Price/Dr Jonathan J Li, Department of Pharmacology, Toxicology and Therapeutics, Mail Stop 1018, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160-7417, USA (Tel: +1-913-5884744; Fax: +1-913-5884740; Email: tprice@kumc.edu; Web: www.kumc.edu/hormonecancers).

8th International Pituitary Congress

New York, USA, 22-25 June 2003.

Contact: Donna Price, 8th International Pituitary Congress Secretariat, BioScientifica Ltd, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642240; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.pituitarycongress2003.com).

National Osteoporosis Society: 9th Bath Conference on Osteoporosis

Bath, UK, 23-26 June 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.nos.org.uk).

Digestive Hormones, Appetite and Energy Balance

London, UK, 30 June-1 July 2003.

Contact: Rachel Boning (Tel: +44-20-83833242; Fax: +44-20-83833142; Email: r.boning@ic.ac.uk; Web: www.obesity.med.imperial.ac.uk).

Biochemical Society Meeting: Stress, Signalling and Control

Colchester, UK, 2-4 July 2003.

Contact: Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW, UK (Tel: +44-20-75803481; Fax: +44-20-76377626; Email: meetings@biochemistry.org; Web: www.biochemistry.org/meetings).

Serono Foundation for the Advancement of Medical Science: Workshop on Inhibins, Activins and Follistatins

Siena, Italy, 3-4 July 2003.

Contact: Pasquale Florio, Obstetrics and Gynecology, University of Siena, Viale Bracci, 53100 Siena, Italy (Tel/Fax: +39-05-77233454; Email: obgyn@unisi.it; Web: www.unisi.it/eventi/inhibin2003).

FEBS 2003: Signal Transduction - from Membrane to Gene Expression, from Structure to Disease

Brussels, Belgium, 4-8 July 2003.

Contact: V Wouters, ICEO (Tel: +32-2-7795959; Fax: +32-2-7795960; Email: febs@iceo.be; Web: www.febs-signal.be).

12th Vitamin D Workshop

Maastricht, The Netherlands, 6-10 July 2003.

Contact: Dr R Bouillon, LEGENDO, Onderwijs en Navorsing (9e Verd), Gasthuisberg, B-3000 Leuven, Belgium (Tel: +32-16-345971; Fax: +32-16-345934; Email: roger.bouillon@medkuleuven.ac.be).

Techniques and Applications of Molecular Biology: a Course for Medical Practitioners

Coventry, UK, 7-10 July 2003.

Contact: Dr Charlotte Moonan, Department of Biological Sciences, University of Warwick, Coventry CV4 7AL, UK (Tel: +44-24-76523540; Fax: +44-24-76523701; Email: charlotte.moonan@warwick.ac.uk).

Bone and Tooth Society Annual Meeting

Sheffield, UK, 9-11 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.batsoc.org.uk).

UK Advanced Postgraduate Diabetes Course

Exeter, UK, 9-11 July 2003.

Contact: Rosemary Sowden, R&D Office, Exeter Postgraduate Medical Centre, Barrack Road, Exeter EX2 5DW, UK (Tel/Fax: +44-1392-403012; Email: rosemary.sowden@rdehc-tr.swest.nhs.uk).

Fertility 2003: Joint Meeting of the Society for Reproduction and Fertility, British Fertility Society and the British Androgen Society,

Aberdeen, UK, 13-17 July 2003.

Contact: Victoria Withy, BioScientifica Ltd, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642219; Fax: +44-1454-642222; Email: fertility2003@endocrinology.org; Web: www.fertility2003.com).

Society for Endocrinology Molecular Endocrinology Workshop

Manchester, UK, 15 July 2003.

Contact: Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

Advances in the Molecular Pharmacology and Therapeutics of Bone Disease

Oxford, UK, 15-16 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.paget.org.uk).

Society for Endocrinology Advanced Endocrine Course

Manchester, UK, 16-17 July 2003.

Contact: Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

International Symposium on Paget's Disease

Oxford, UK, 16-19 July 2003.

Contact: Janet Crompton, The Old White Hart, North Nibley, Dursley GL11 6DS, UK (Tel: +44-1453-549929; Fax: +44-1453-548919; Email: janetcrompton@compuserve.com; Web: www.paget.org.uk).

Society for Endocrinology Clinical Practice Day

Manchester, UK, 18 July 2003.

Contact: Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm)

56th Harden Conference: Biological Electron and Proton Transfer

Plymouth, UK, 26-30 August 2003.

Contact: The Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW, UK (Tel: +44-20-75803481; Fax: +44-20-76377626; Email: meetings@biochemistry.org; Web: www.biochemistry.org/meetings).

4th Royan International Research Award

Tehran, Iran, September 2003.

Contact: Secretariat, PO Box 19395-4644, Tehran, Iran (Tel: +98-21-2413790/2411592-4; Fax: +98-21-2409314; Email: info@royaninstitute.org; Web: www.royaninstitute.org).

57th Harden Conference: Proteinase Structure and Function

Oxford, UK, 9-13 September 2003.

Contact: The Meetings Office, Biochemical Society, 59 Portland Place, London W1B 1QW, UK (Tel: +44-20-75803481; Fax: +44-20-76377626; Email: meetings@biochemistry.org; Web: www.biochemistry.org/meetings).

Society for Endocrinology Endocrine Nurses Training Course: The Pituitary Gland

Durham, UK, 10-12 September 2003.

Contact: Ann Lloyd, Society for Endocrinology, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642200; Fax: +44-1454-642222; Email: info@endocrinology.org; Web: www.endocrinology.org/sfe/train.htm).

6th International Workshop: Resistance to Thyroid Hormone

Miami Beach, FL, USA, 13-16 September 2003.

Contact: Paul M Yen (Fax: +1-301-4024136; Email: pauly@intra.niddk.nih.gov) or Sheue-Yann Cheng (Email: sycheng@helix.nih.gov).

Oxford Advanced Endocrinology Seminar

Oxford, UK, 16-17 September 2003.

Contact: Helen Gregson, BioScientifica Ltd, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642212; Fax: +44-1454-642222; Email: conferences@endocrinology.org).

75th Annual Meeting of the American Thyroid Association

Palm Beach, FL, USA, 16-21 September 2003.

Contact: ATA, 6066 Leesburg Pike, Suite 650, Falls Church, VA 22041, USA (Email: admin@thyroid.org; Web: www.thyroid.org).

ESPE 2003: 42nd Annual Meeting of the European Society of Paediatric Endocrinology

Ljubljana, Slovenia, 18-21 September 2003.

Contact: Congrex Sweden AB, Attn: ESPE 2003, Karlavägen 108, Elevator V, 8th Floor, PO Box 5619, SE-114 86 Stockholm, Sweden (Tel: +46-8-4596600; Fax: +46-8-6619125; Email: espe2003@congrex.se; Web: www.eurospe.org/meetings.jsp).

25th Annual Meeting of the American Society for Bone and Mineral Research

Minneapolis, MN, USA, 19-23 September 2003.

Contact: ASBMR, 2025 M Street, NW Suite 800, Washington DC 20036-3309, USA (Tel: +1-202-3671161; Email: asbmr@dc.sba.com; Web: www.asbmr.org).

3rd International Symposium on Testosterone: Action, Deficiency, Substitution

Castle Elmau, Bavaria, Germany, 25-28 September 2003.

Contact: Prof. Dr E Nieschlag, Institute of Reproductive Medicine of the University of Münster, Domagkstr 11, D-48129 Münster, Germany (Tel: +49-251-8356096; Fax: +49-251-8356093; Email: nieschl@uni-muenster.de or olerink@uni-muenster.de).

Advances in Anti-Ageing

London, UK, 27 September 2003.

Contact: Institute of Cosmetic and Reconstructive Surgery (Tel: +44-20-87356060; Fax: +44-20-89940801; Email: enquiries@plasticsurgerypart.org.uk).

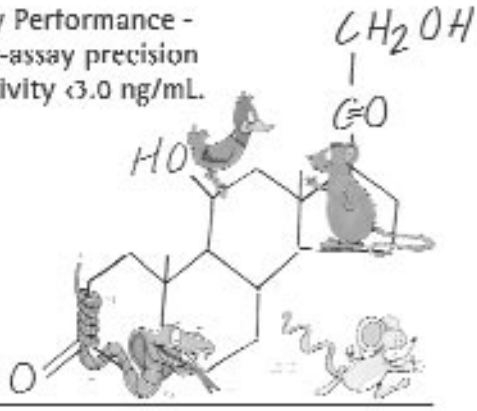
11th EFES Postgraduate Course in Clinical Endocrinology

Oxford, UK, 29 September-1 October 2003.

Contact: Helen Gregson, BioScientifica Ltd, 22 Apex Court, Woodlands, Bradley Stoke, Bristol BS32 4JT, UK (Tel: +44-1454-642212; Fax: +44-1454-642222; Email: conferences@endocrinology.org; Web: www.euro-endo.org/courses.htm).

Corticosterone DIRECT ELISA

- Non-extraction - A simple dilution step replaces tedious solvent extraction/evaporation.
- Non-isotopic - Ideal for use in any laboratory. Avoids radioactive regulations; longer shelf-life.
- Application - Suitable for mouse and rat (and bird, reptile & amphibia) serum and plasma samples.
- Small Sample Volume - 30 µL for duplicate determination.
- Wide Working Range - 15-1800 ng/mL.
- Convenient - Easy to use microlitre strip format and 12 months shelf life.
- Excellent Assay Performance - Intra and Inter-assay precision C.V. 8%, sensitivity <3.0 ng/mL.



POMC ELISA

- The first commercial kit for ACTH precursors (POMC and pro-ACTH)
- 20 µL EDTA plasma sample requirement, simple overnight protocol.
- Wide working range: 12-1200 pmol/l.
- Two-site assay: Monoclonal antibodies confer excellent specificity.
- Good Assay Performance : Intra-assay precision <8%, Inter-assay precision <12%, sensitivity <12pmol/L.
- Minimal hands on time : Results available next day.
- Convenient 12 x 8-well strips for economy and convenience.
- Robust, non-isotopic format, 12 months shelf life.

Contact IDS now for further details and to discuss an evaluation!

www.idsltd.com

IDS Ltd, 10 Didcot Way, Boldon Business Park, Boldon, Tyne & Wear, NE35 9PD, UK
Tel: +44 (0) 191 519 0660 Fax: +44 (0) 191 519 0760 e-mail: marketing@idsltd.com

BEST OF BES 2003
GOOD TIMES IN GLASGOW!


A spoonful of sugar...

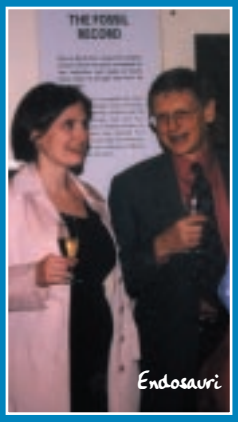

Cheers from the Editor


Bumps at BES!


Step on my toe again Steve, and you're sacked!


The BES, a time for reflection


A bunch of jolly Endos


Endosauri


Pipers at the posters


You put your left leg in, your left leg out...


The Clan


Celebrations take their toll...